I. REMARKS

Claims 25-27 and 43-66 are presently pending in this application. Claims 46-54 have been withdrawn pursuant to a restriction requirement. Claims 25-27, 43-45 and 55-66 stand variously rejected under 35 U.S.C. §§ 102 and 103. Reconsideration of the application is requested in view of the following remarks.

Rejections Under 35 U.S.C. § 102

Claims 25-27, 43-45 and 55-57 are rejected under 102(b) as allegedly anticipated by Heldin et al. (Nature 319:511-514, 1986, hereinafter "Heldin"). In support of this allegation, the Office asserts that Applicants have not offered any comparative evidence establishing a patentable distinction between their recombinantly produced protein and the isolated protein of the reference. (Final Office Action, page 3). In particular, the Office continues to assert that (1) the protein preparation of the reference appears to be homogenous; (2) the reference states that one homogenous compound was obtained and (3) no other amino acid sequences were obtained. (Final Office Action, page 4).

Applicants traverse the rejection and supporting remarks.

Contrary to the Office's assertions, the record is replete with evidence establishing that Heldin's non-recombinant methods of protein production "cannot result in a protein product free of contaminating human proteins." (see, *e.g.*, Cousens and Betsholtz Declarations). Indeed, both the Cousens and Betsholtz Declarations of record directly refute each and every assertion made by the Office. First, both Declarations establish that Heldin's protein preparations are *not* homogenous for human PDGF (*see, e.g.*, Cousens, paragraph 3; Betsholtz, paragraphs 4-6). Second, the Declarations demonstrate that one of skill in the art would not interpret Heldin's statement regarding homogeneity of the isolated protein as meaning that the protein preparations that are free of other human proteins (see, *e.g.*, Cousens, paragraph 3). Finally, Drs. Cousens provides explanatory evidence addressing why Heldin failed to obtain amino acid sequence from the

contaminating human proteins necessarily present in their protein preparation (*see,* Cousens Declaration, paragraph 6). Further evidence of record establishes that, prior to the present invention, significant amounts of human PDGF could not be readily isolated. (*see, e.g.,* Betsholtz Declaration). Thus, the evidence of record leads to only one possible conclusion -- Heldin's protein preparation is not free of other human proteins and, accordingly, is distinct from the claimed invention.

In sum, the record demonstrates that the claimed invention is distinguishable from the protein preparation disclosed in Heldin. Accordingly, claims 25-27, 43-45 and 55-57 are not anticipated by this reference and withdrawal of this rejection is respectfully requested.

Rejections Under 35 U.S.C.§ 103(a)

Claims 55-57 stand rejected as allegedly obvious over Heldin. It is maintained that the facts of record support a conclusion that the PDGF preparation of the reference is not different from that which is claimed and that "Applicant has not addressed the obviousness of the pharmaceutical compositions, but rather is arguing the nature of isolated PDGF." (Final Office Action, page 5).

Applicants traverse the rejection and supporting remarks.

The claims at issue are directed to recombinant protein preparations of PDGF A-chain homodimers (produced in a non human cell such that the protein preparation is free of other human proteins) in combination a pharmaceutically acceptable excipient. Thus, the statutory inquiry of obviousness necessarily requires a determination of what the reference teaches or suggests about recombinant PDGF proteins. Indeed, as acknowledged by the Office (Final Office Action, page 5), disclosure of an isolated protein does not necessarily render obvious a recombinantly produced protein. *see, e.g., Ex parte Goeddel,* at 5 USPQ2d 1449 (BPAI, 1987). A correct obviousness inquiry in such situations also examines whether the applicant has established that there are

sufficient differences between isolated and recombinantly produced proteins.

Pursuant to these standards, Applicants have previously and repeatedly addressed the rejections under section 103 by pointing out (1) that the reference does not teach or suggest the use or the desirability of recombinantly produced PDGF preparations and (2) that the protein preparation of the claimed invention is different in several important respects from that disclosed in the reference. The failure of the cited reference to teach or suggest that it would be desirable to use recombinantly produced protein has been well-documented throughout prosecution. (see, *e.g.*, Response filed December 3, 1999). With regard to distinguishing the protein preparations the evidence of record (for example the Cousens and Betsholtz declarations) demonstrates that, in direct contrast to the claimed invention, Heldin's protein preparation is simply not free of other human proteins. Applicants submit that the lack of other human proteins in the claimed invention makes it distinguishable from the protein preparation disclosed in Heldin.

In sum, since Heldin is silent as to recombinantly produced proteins and since the record has established the difference between the claimed protein and that of Heldin, Applicants again submit that an obviousness rejection is improper and should be withdrawn.

II. CONCLUSION

In view of the foregoing, Applicants submit that the claims are now in condition for allowance and request early notification to that effect.

Please direct all further communications regarding this application to:

Lisa E. Alexander, Esq.
CHIRON CORPORATION
Intellectual Property - R440
P.O. Box 8097
Emeryville, CA 94662-8097
Telephone: (510) 923-2585
Facsimile: (510) 655-3542.

Respectfully submitted,

Date: July 20, 2000

By: D Pasternak
Dahna S. Pasternak
Registration No. 41,411
Attorney for Applicants

CHIRON CORPORATION
Intellectual Property - R440
P.O. Box 8097
Emeryville, CA 94662-8097
Telephone: (510) 923-2585
Facsimile: (510) 655-3542